below, the Applicant believes that claims 50, 59, 63 and 64 are now in condition for allowance and, therefore, claims 65-68 should be rejoined as a method of using a patentable agent. If, however, the Patent and Trademark Office determines that claims 65-68 should not be maintained in this application for any reason, the Applicant authorizes the Patent and Trademark Office to cancel claims 65-68.

With Respect to the Objections to the Drawings:

Figure 1 and Figure 2 stand objected to for the reasons indicated on the Notice of Draftsperson's Patent Drawing Review. Replacement figures are attached to this Response and Amendment. Withdrawal of the objections to the figures is requested.

With Respect to the Rejections Under 35 U.S.C. §112:

Claims 50-64 stand rejected under 35 U.S.C. §112 for the reasons indicated on page 4, paragraph 2 of the Office Action. Claims 50-62 have been amended. Support for these amendments can be found at page 17, line 25 through page 18, line 8, among other places. Withdrawal of these rejections is requested.

With Respect to the Rejections under 35 U.S.C. §102:

Claims 50, 51, 58 and 63 stand rejected under 35 U.S.C. §102 as being anticipated by Gonzalez et al. for the reasons indicated on page 5, paragraphs 2-3 of the Office Action. Claim 50 has been amended to add the limitation "where the antigen elicits a protective response to the disease." Support for this limitation can be found at page 21, lines 16-27. As stated in the Gonzalez reference in the abstract, lines 6-9:

> ...The hybrid polypeptide was shown to induce high titers of serum antibodies (Ab) against CTB and the synthetic VP4 peptide following subcutaneous immunization; paradoxically, however, the Ab obtained did not recognize the virus by an enzyme-linked immunosorbent assay method, nor had detectable neutralizing activity....

Hence, the Gonzalez reference does not anticipate claim 50 as amended. Claims 51 and 58 depend on claim 50. Claim 63, has been amended to include the limitations of claim 50. Therefore, withdrawal of this rejection is requested.

Claims 50, 53, 54 and 63 stand rejected under 35 U.S.C. §102 as being anticipated by Hajishengallis et al. for the reasons indicated on page 5, paragraphs 4-5 of the Office Action. Claim 50, as currently amended, reads as follows:

> A protein complex comprising five monomeric fusion proteins;
> where each fusion protein comprises a cholera toxin B subunit linked to a first immunogenic antigen from a causal factor of a first mammalian disease; and
> where the antigen elicits a protective response to the disease.

By contrast, as disclosed in the Hajishengallis reference in the cited passages, pages 4322-4323, 4330 last paragraph and Fig. 1, merely discloses a pentamer of CTB linked to an antigen through a truncated CLARE TAYLOR subunit. It does not disclose "a protein complex comprising **five monomeric fusion proteins**, where **each fusion protein** comprises a cholera toxin B subunit linked to a first immunogenic antigen," emphasis added, as recited in claim 50; that is, where the protein complex comprises not only five CTB subunits, but five antigens as well. Hence, the Hajishengallis reference does not anticipate claim 50 as amended. Claims 53 and 54 depend on claim 50. Claim 63, has been amended to include the limitations of claim 50. Therefore, withdrawal of this rejection is requested.

With Respect to the Rejections under 35 U.S.C. §102(e):

Claims 50, 53, 54, and 63 stand rejected under 35 U.S.C. §102(3) as being anticipated by Russell US 6,030,624. The Patent and Trademark Office stating:

> Russell teaches a fusion protein that encodes colera [sp] toxin A2 and B subunits along with an immunogenic antigen to a mammalian disease (col 10, lines 11-28).

The entire text of the cited passage is as follows:

> Thus, the present invention is directed to a plasmid capable of replication in a host which comprises, in operable linkage: a) an origin of replication; b) a promoter; and c) DNA sequences encoding the A2 subunit of cholera toxin. In addition, the plasmid may further comprise DNA sequences encoding subunit B of cholera toxin fused to the A2 subunit of cholera toxin. One such preferred plasmid is $pCT^{\Delta A1}$ (deposited with ATCC, 10801 University Blvd., Manassas, Va. 20110-2209 on May 4, 1999, designation PATENT TERM ADJUSTMENT-4). In another embodiment, the plasmid further comprises salivary binding protein (SBR) from Streptococcus mutans surface protein (AgI/II) fused to the A2 subunit of cholera toxin. One such preferred plasmid is designated pSBR-CTA2/B or $pSBR\text{-}CT^{\Delta A1}$ (deposited with ATCC, 10801

University Blvd., Manassas, Va. 20110-2209 on May 4, 1999, designation PATENT TERM ADJUSTMENT-5).

Claim 50, as currently amended, reads as follows (emphasis added):

> **A protein complex comprising five monomeric fusion proteins**;
> where each fusion protein comprises a cholera toxin B subunit linked to a first immunogenic antigen from a causal factor of a first mammalian disease; and
> where the antigen elicits a protective response to the disease.

The cited passage from the '624 Patent does not appear to disclose or suggest "a protein complex," in any form. Claims 53 and 54 depend on claim 50. Claim 63, has been amended to include the limitations of claim 50. Therefore, withdrawal of this rejection is requested.

With Respect to the Rejections under 35 U.S.C. §103:

Claim 52 stands rejected under 35 U.S.C. §103 as being unpatentable over Gonzalez and further in view of Manson et al. for the reasons indicated on pages 6 through 7 of the Office Action. Claim 52 depends on claim 50. For the reasons indicated above, claim 50 is believed to be patentable. Therefore, this rejection is believed to be moot and withdrawal of this rejection is requested.

CONCLUSION

For the reason stated above, the Applicant respectfully believes that all pending claims, claims 50-86, are in condition for allowance and a Notice of Allowance is earnestly solicited. If, however, there remain any issues that can be resolved by telephone with the Applicants representative, the Examiner is encouraged to contact the undersigned directly.

Please charge all fees due in connection with this communication, including the fee for a one month extension of time to respond. However, if any fee is due, the Commissioner is hereby authorized to charge payment of the fee associated with this communication to Deposit Account No. 19-2090.

Respectfully submitted,

SHELDON & MAK
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Date: January 21, 2003 By _____
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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

Cancel claims 1-49.

Amend claims 50-62 as follows:

50. (Amended) [A fusion protein comprising a multimeric] A protein complex comprising five monomeric fusion proteins;

where each fusion protein comprises a cholera toxin B subunit [and] linked to a first immunogenic antigen from a causal factor of a first mammalian disease; and

where the antigen elicits a protective response to the disease.

51. (Amended) [The fusion protein] The protein complex of claim 50, where the first immunogenic antigen is a rotavirus antigen.

52. (Amended) [The fusion protein] The protein complex of claim 50, where the first immunogenic antigen is an enterotoxigenic *E. coli* antigen.

53. (Amended) [The fusion protein] The protein complex of claim 50, [can further comprise] further comprising a second cholera toxin subunit.

54. (Amended) [The fusion protein] The protein complex of claim 53, where the second cholera toxin subunit is cholera toxin A2 subunit.

55. (Amended) [The fusion protein] The protein complex of claim 50, [can further comprise] further comprising a second immunogenic antigen from a causal factor of a second mammalian disease.

56. (Amended) [The fusion protein] The protein complex of claim 55, where the second immunogenic antigen is a rotavirus antigen.

57. (Amended) [The fusion protein] The protein complex of claim 55, where the second immunogenic antigen is an enterotoxigenic *E. coli* antigen.

58. (Amended) [The fusion protein] The protein complex of claim 50, where the first mammalian disease is an infectious enteric disease.

59. (Amended) [The fusion protein] The protein complex of claim 50, further comprising a cholera toxin A2 subunit[, a multimeric cholera toxin B subunit, a first immunogenic antigen from a causal factor of a mammalian disease, and] linked to a second immunogenic antigen from a causal factor of a [second] mammalian disease.

60. (Amended) [The fusion protein] The protein complex of claim 59, where the first immunogenic antigen is a rotavirus antigen.

61. (Amended) [The fusion protein] The protein complex of claim 59, where the second immunogenic antigen is an enterotoxigenic *E. coli* antigen.

62. (Amended) [The fusion protein] The protein complex of claim 59, where the first mammalian disease or the second mammalian disease or both the first mammalian disease and the second mammalian disease is an infectious enteric disease.

63. (Amended) A [fusion protein] protein complex encoded by [the DNA construct of claim 1] a DNA construct that encodes, upon expression in a plant cell, a protein complex comprising five monomeric fusion proteins;

where each fusion protein comprises a cholera toxin B subunit linked to a first immunogenic antigen from a causal factor of a first mammalian disease; and

where the antigen elicits a protective response to the disease.

64. (Amended) A [fusion protein] protein complex encoded by [the DNA construct of claim 1] a DNA construct that encodes, upon expression in a plant cell, a protein complex comprising:

a) five monomeric fusion proteins, where each fusion protein comprises a cholera toxin B subunit linked to a first immunogenic antigen from a causal factor of a first mammalian disease, and where the antigen elicits a protective response to the disease; and

b) a cholera toxin A2 subunit linked to a second immunogenic antigen from a causal factor of a mammalian disease.

65. A method of inducing partial or complete immunity to an infectious disease in a mammal comprising providing to the mammal for oral consumption an effective amount of the fusion protein of claim 50.

66. A method of inducing partial or complete immunity to an infectious disease in a mammal comprising providing to the mammal for oral consumption an effective amount of the fusion protein of claim 59.

67. A method of inducing partial or complete immunity to an infectious disease in a mammal comprising providing to the mammal for oral consumption an effective amount of the fusion protein of claim 63.

68. A method of inducing partial or complete immunity to an infectious disease in a mammal comprising providing to the mammal for oral consumption an effective amount of the fusion protein of claim 64.

Add new claims 69-86

69. The protein complex of claim 63, where the first immunogenic antigen is a rotavirus antigen.

70. The protein complex of claim 63, where the first immunogenic antigen is an enterotoxigenic *E. coli* antigen.

71. The protein complex of claim 63, further comprises a second cholera toxin subunit.

72. The protein complex of claim 71, where the second cholera toxin subunit is cholera toxin A2 subunit.

73. The protein complex of claim 63, further comprises a second immunogenic antigen from a causal factor of a second mammalian disease.

74. The protein complex of claim 73, where the second immunogenic antigen is a rotavirus antigen.

75. The protein complex of claim 73, where the second immunogenic antigen is an enterotoxigenic *E. coli* antigen.

76. The protein complex of claim 63, where the first mammalian disease is an infectious enteric disease.

77. The protein complex of claim 63, further comprising a cholera toxin A2 subunit linked to a second immunogenic antigen from a causal factor of a mammalian disease.

78. The protein complex of claim 77, where the first immunogenic antigen is a rotavirus antigen.

79. The protein complex of claim 77, where the second immunogenic antigen is an enterotoxigenic *E. coli* antigen.

80. The protein complex of claim 77, where the first mammalian disease or the second mammalian disease or both the first mammalian disease and the second mammalian disease is an infectious enteric disease.

81. The protein complex of claim 64, where the first immunogenic antigen is a rotavirus antigen.

82. The protein complex of claim 64, where the first immunogenic antigen is an enterotoxigenic *E. coli* antigen.

83. The protein complex of claim 64, where the second immunogenic antigen is a rotavirus antigen.

84. The protein complex of claim 64, where the second immunogenic antigen is an enterotoxigenic *E. coli* antigen.

85. The protein complex of claim 64, where the first mammalian disease is an infectious enteric disease.

86. The protein complex of claim 77, where the second mammalian disease is an infectious enteric disease.